ILLUSTRATIVE CASES

An Austrian observer had a case of an infant of 6 months, severely ill with high temperature, but showing no physical signs. The tympanic membranes were so nearly normal that he hesitated to open them, but did so; a very little pus escaped. The infant did not improve. He then opened both mastoids, which were found full of pus, and the infant immediately improved.

I had a similar experience with a child just over the infant's age (but this does not affect the case). He had a severe infection, probably influenzal, with a temperature of 103° to 105° for more than a week. A physician was unable to find anything wrong. The tympanic membranes were apparently normal, but nevertheless incisions were made. Even with a magnifying auriscope scarcely any secretion was seen, though twelve hours later a small amount of pus was observed in the meatus. No improvement followed, and twenty-four hours later both mastoids were opened and found to contain pus. Thereafter recovery began. It is almost certain that the mastoid suppuration was present before any otitis media, and infection may well have arrived via the blood stream. In support of this is the fact that the child had a low red cell blood count and only 6,500 leucocytes, suggesting the resistance was much lowered. It is possible this was a pneumococcal case.

The second group of pseudo-latent cases are those associated with diarrhoea and vomiting. This parenteral otitis media is to be dealt with by a subsequent speaker. I propose, therefore, only to quote a case which has recently been under my observation and which illustrates some of the typical features.

An infant of 9 months was admitted to Guy's Hospital on account of diarrhoea and vomiting. It was said to have had otitis media, from which it recovered fourteen days before admission. Diarrhoea and vomiting began one week later. The child was very ill and wasted. In the stools were found *Bacillus coli communis* and *Streptococcus brevis*. Twelve days after admission the left ear discharged pus. The following day examination showed the right membrane bulging; incision released pus, but no improvement followed. Therefore on the following day both mastoids were rapidly opened; the left one contained pus, the right antrum a little muco-pus only. The infant survived four to five days.

Post-mortem examination showed bronchopneumonia, follicular enteritis, and colitis, as well as the presence of pus in the mastoids, as at operation. No doubt the serious condition of the child led to concentration on treatment. Only discharge of pus from one ear led to examination of the ears. Even though the anaesthetic given was minimal, bronchopneumonia supervened.

TUBERCULOUS OTITIS MEDIA

It is always stated that this disease is common in infants. One observer (Logan Turner) stated that of cases of otitis media in infants under 1 year, 50 per cent. were tuberculous; others state that tuberculosis accounts for a large percentage in infants. Mygind, in 1922, in a review of 1,000 mastoid operations, found that in only 1.4 per cent. of the children were tubercle bacilli present in the pus, but considered that this figure greatly underestimated the frequency in children. All are agreed that when tuberculous otitis media does occur the prognosis is much better in the healthy than in the unhealthy. In my experience tuberculosis of the middle ear is not common in infants, and I suggest that it is a tradition to state it is so common. There is, of course, the possibility that it is getting less frequent with improvement in living conditions.

Tuberculous otitis media causes extensive destruction of the temporal bone; the facial nerve becomes involved; the labyrinth is attacked; and the glands about the ear enlarge and may break down. Sometimes both ears are affected, and double facial paralysis results. Operation may disclose so much disease that the dura mater is exposed and the labyrinth has become a sequestrum. On one occasion removal of the cochlea was followed by a flow of cerebro-spinal fluid from the internal auditory meatus and continued for ten days; it then ceased, and the child made a good recovery. Infection is no doubt generally from milk, but not always so, since cases are seen in breast-fed infants, even with healthy mothers.

When tuberculous otitis media is diagnosed a thorough mastoid operation should be performed, and gives a very good prospect of recovery.

SENESCENCE *

BY

G. P. BIDDER, Sc.D.

Men, dogs, and horses show with age symptoms whose onset is conveniently called senescence; water voles, female plaice, sea anemones, and the bath sponge do not show senescence. I have suggested that senescence is the after-result of the mechanism which secures specific size.†

Minot concluded all cells to be senescent until they are rejuvenated by increase of nuclear substance, as effected in the ovum dividing after fertilization; the daughter cells subsequently increase cell body and return to senescence. Child writes (*Senescence and Rejuvenescence*, 1915, p. 460): "When the organism is adding to its structural substance, and transformation from more active to less active physical and chemical conditions takes place, senescence occurs"; he conditionally approves (p. 275) Minot's statement, "the rate of senescence is highest in youth and lowest in advanced life." Both views appear contradicted by the British Museum section of a giant redwood, felled with 1,335 rings of healthy wood, and by the giant cypress of Mexico (*Kew Bulletin*, 1922, p. 199), producing annual leaves and fruit in vigour, unimpaired by 5,000 years of cell division. Woodruff's paramecium culture has divided for more than twenty-one years without conjugation. Carrel's seventeen-year-old culture of cells from a chick heart, following Loeb's experiments on tumours, convinced Raymond Pearl (*Biology of Death*, p. 30) "that death is not a necessary inherent consequence of life in the somatic cell."

Pseudo-senescence and pseudo-specific size are often mere consequences of the decrease in ratio of surface to volume as size increases. Bath sponges stop growth at about thirty inches diameter, but grow on vigorously if divided with a knife into four-inch cubes (L. R. Crawshay, *Reports on Sponge Fisheries*, Colonial Office, 1925 *et sqq.*). Having no nervous system, interior cells cannot be rejuvenated by the knife. The flagellate cells must always draw in water through the surface and eject it through the large holes; with increase in size the relative diminution in surface requires higher velocity to feed the sponge, lengths of all channels are increased, and consequent friction becomes more than the flagella can overcome. Vegetative masses, aggregates of protozoa, tumours—all tend to be limited in size by necrosis of parts far removed from the surface.

For Child (p. 438), "biological importance of the relation between surface and volume rests rather upon a process of logic than upon the data of observation." But he records valuable experiments on change of size in flatworms, showing that rate of metabolism is always more rapid for the smaller worms. Analysis of his results shows that rate of metabolism varies inversely as length of the animal. His experiments prove, therefore, that rate of metabolism varies as ratio of respiratory surface to volume of tissue.

* Paper read in opening a discussion in the Section of Comparative Medicine at the Centenary Meeting of the British Medical Association, London, 1932.

† *Proc. Linn. Soc.*, 1925, p. 17, and 1926, p. 19; *Nature*, 1925, cxv, 156; British Association Report, 1927 (Leeds), p. 64.

May progressive retardation of cell division in the larva be due to multiplication of cell walls impeding transference of oxygen and food? Measurement of senescence by interval of time between cell divisions leads to strange paradoxes about the newborn babe,† whose brain cells never divide again, while the epidermis continues rapid division for eighty years. Considering Calkin's (1926) view of endomixis, it seems strange that paramecium cannot live a day without rejuvenescence by rearrangement, while brain cells which govern this country have lived so for 20,000 days. I suggest that we were not born with infinitely senescent brains and rejuvenated epithelium ; rapidity of division in our skin has been evolved to keep it clean and whole ; undivided brain cells have been evolved because their function is to remember.

Child (p. 302) writes, with what seems inconvenient use of words, of the insects and fish whose death follows first extrusion of sexual products, that " the organism is undoubtedly in an advanced stage of senescence when sexual maturity is attained." The tissues of the Pacific salmon have come into being to be converted into reproductive cells—the conversion is essential to survival of the salmon's progeny ; the moment of its fulfilment is climax of the parent's life. Senescence in man did not conduce to survival of our early ancestors, and it is the anticlimax of our life. *Parental death* (*Nature,* cxv, 495), as aim and purpose of somatic life, is ancient and historic " natural " death. We will recall briefly stages of its evolution in various lines of descent.

Fission of a protozoon results in two living protozoa ; but encystment and spore formation ends in escaping spores leaving an empty spore case, inside which often residual protoplasm adheres: this is the first somatic corpse. Among sponges, Grantia in midsummer at Plymouth is full of embryos almost ready to escape ; each escaping larva tears the flagellate epithelium ; the tattered and exhausted maternal remains disappear: September's rocks show only numerous minute young sponges (*Q.J.M.S.*, xxxviii, 11). Similar parental death awaits proglottides of the tapeworm, but here the cast-off envelope of the undying protozoan ova has reached metazoan grade. Higher still in grade are the swollen bodies of marine worms, and ephemeral imagines of insects ; and very interesting parental deaths are those of the eels. Johannes Schmidt discovered how the common eel leaves our ponds and crosses the Atlantic to spawn and die in the western sea of its origin. Flower (*Proc. Zool. Soc.,* 1925, p. 259) states that it lives fifty years when prevented from doing this ; the degeneration of tissues is therefore *not* caused by bodily senescence, but by the sexual crisis. Cunningham (*Journ. Mar. Biol. Assoc.,* 1892, ii, 29) studied this crisis in conger eels: when the gonads begin ripening, the conger, male or female, ceases feeding for six months ; the ovary swells, while viscera, muscles, bones, and teeth degenerate ; a scalpel cuts through the whole skull like cheese. Cunningham found no ovary weighing more than 0.22 of the gravid weight, but he quotes records of ovaries forming 0.35 and 0.46 of the gravid weight. The figures suggest that a vertebrate cannot continue to live after the loss of some 40 per cent. of the substance of the body.* Pacific salmon show similar increase of the gonads at the expense of mortal degeneration.

* Rugen and Stoessiger, (*Annals of Eugenics,* 1927, p. 76) give statistics of muscular strength, nervous control, and breathing capacity, from which I suggest the conclusion that the organs of exceptionally well-preserved men of 80 contain about 35 per cent. less protoplasm than they did at 27, indicating that with loss of 40 per cent. of its protoplasm the human body cannot resist minimal accident. Child's Planaria lost 99 per cent. without injury, showing a compensatory advantage for races which have refused the support or protection of a skeleton ; they survive starvation by resuming infantile size.

For preservation of the species there has been evolved this process, by which each soma shall accumulate for the species from food as much capital as is possible. This capital shall not be continuously risked on the chances attending one life, but when sufficient has been accumulated it shall be distributed, so that, with differing accidents, probably two of the offspring may survive to continue the race. Yet the processes above reviewed are primitively wasteful of the property of the species, since three-fifths of the capital is lost in the parental corpse. We know many other species which receive further advantage from evolution of processes economizing this loss.

In fresh-water sponges many encased gemmules winter in the ruins of their parent ; with spring their issuing amoeboid cells grow up in a coalescing mass which envelops and utilizes the maternal skeleton (Potts, *Fresh Water Sponges,* 1887, pp. 215, 259; Carter, *Journ. Bombay Branch Roy. Asiatic Soc.,* 1849, xii,* 45). Many female spiders economize somatic tissues of the male, for his offspring, by eating him. When the Atlantic salmon ascends our rivers to spawn, tissues are degenerated for benefit of the gonads almost as in his Pacific cousin ; but the spent body does not completely die, and, half swimming, half drifting, reaches the sea, feeds again, and in a few years returns much grown, with very much larger gonads (never over 30 per cent. of total weight) ; after other years it may return a third time. Comparison is obvious with annual plants, some strains of which grow from the root a second or even a third year, but in the salmon the whole parental envelope is economized.

Male plaice are fertile at 5 or 6 years old ; not being caught above 8 years old (Wallace, *Fishery Investigations,* 1914, Ser. ii, vol. ii, p. 12) they probably die after spawning, not always after first spawning. Their economy is unimportant, since plaice do not pair. Parental death has disappeared in the valuable female. She matures at 6 or 7 years old ; at 25 (some 55 years old for humanity) she is 70 per cent. longer and five times heavier ; plaice of unknown age are recorded up to twelve times average weight at first maturity, and over twice the length.† We have no evidence of her senescence, nor of any cause of death except violence. Her species seems to have achieved the perfect economy of an undying and ever-fertile parental envelope.

Mammals, like the female plaice, have lost parental death, but the parental envelope is not undying. Man only grows about 18 per cent. in length and 75 per cent. in well-trained weight after puberty, shrinking in both after twice that age at a rate which increases every year. In sea or land the most natural animal death is to be killed and eaten ; but adult wolf or primitive man lives in increasing danger of feeding a *younger* adult of his own species ; adult cod or squid live in diminishing danger of being eaten by older adults of their own species. In water cannibalism by the old, rare specific size, and rare senescence contrast on land with cannibalism by the young, general specific size, and frequent senescence. Are not these differences correlated?

Galileo (vide D'Arcy Thompson, *Growth and Form,* p. 21) showed it impossible for a swiftly moving animal on land to increase its size in the same proportion of parts and to maintain its agility. Lankester (*Comparative Longevity,* p. 37) quotes Herbert Spencer's statement of this principle: increase in size increases weight as the cube of the length, but areas of cross-sections of muscles

* Misprinted " iii " in Vosmaer's *Bibliography of Sponges.*

† Since growth in plaice depends entirely on quantity of nourishment, it appears likely that a limiting size may be reached when area of gut surface is only sufficient to nourish mass of body, and cannot provide for increase. Rubner's experiments (quoted by Child, p. 272) suggest that this relative reduction of feeding surface may explain much slowing down in growth as size increases, and some pseudo-specific size.

and bones only as the square of the length ; so that, if an animal doubles its length without alteration of proportions, " its ability to overcome forces has quadrupled, the forces it has to overcome have grown eight times as great." " But," writes D'Arcy Thompson, " as Galileo also saw, if an animal be wholly immersed in water, . . . then the weight is counterpoised to the extent of an equivalent volume of water. . . . Under these circumstances there is no longer a physical barrier to the indefinite growth in magnitude of the animal."

Giant trees, cultures of chick cells and of paramecium, measurements of plaice and of sponges, all indicate that indefinite growth is natural. Galileo proved it fatal to swiftly moving land animals, therefore swiftly moving mammals and birds were impossible until their ancestors had evolved a mechanism for maintaining specific size within an error not impairing adequate efficiency. Even without evidence of ever-growing organisms, we could not suppose that the close correspondence to specific size, which we see in all swiftly moving creatures of earth or air, results from mere " senescent " fading-out of the zygotic impulse to cell division and cell increase. Specific size is probably most important to birds, with their aeroplane mechanics strictly enjoining conformity of scale to plan ; but to men it is most noticeable in man. Only familiarity prevents marvel at the rarity of meeting a man more than 20 per cent. taller or shorter than 5½ ft., or of discovering his remains in any place, of any race, of any epoch. Probably our erect posture enforces accurate proportions of length to weight, for running.

Adequate efficiency could only be obtained by the evolution of some mechanism to stop natural growth so soon as specific size is reached. This mechanism may be called the regulator, avoiding the word " inhibitor " so as not to connote a physiological assumption. However ignorant we are of its nature, its action is traced in anthropometric statistics: a steady diminution in growth rate from a maximum at puberty to vanishing-point in the twenties. That the regulator works through change in the constitution of the blood is shown by the perpetual division of Carrel's chick cells in embryonic plasma, whereas cell division is ended in the heart of a hen.

I have suggested that senescence is the result of the continued action of the regulator after growth is stopped. The regulator does efficiently all that concerns the welfare of the species. Man is within 2 cm. of the same height between 18 and 60, he gently rises 2 cm. between 20 and 27, and still more gently loses 1 cm. by 40 or thereabouts. If primitive man at 18 begat a son, the species had no more need of him by 37, when his son could hunt food for the grandchildren. Therefore the dwindling of cartilage, muscle, and nerve cell, which we call senescence, did not affect the survival of the species ; the checking of growth had secured that by ensuring a perfect physique between 20 and 40. Effects of continued negative growth after 37 were of indifference to the race ; probably no man ever reached 60 years old until language attained such importance in the equipment of the species that long experience became valuable in a man who could neither fight nor hunt. This negative growth is not the manifestation of a weakness inherent in protoplasm or characteristic of nucleated cells ; it is the unimportant by-product of a regulating mechanism necessary to the survival of any race of swiftly moving land animals, a mechanism evolved by selection and survival as have been evolved the jointing of mammalian limbs, and with similar perfection.

(NOTE.—Though Galileo's law is the usual cause of the evolution of specific size, with consequent senescence, there are other causes. Mrs. Sexton, of the Marine Biological Association, told me that in her sand-hopper cultures both females and males eventually stop breeding and growing, and die of old age. Probably many animals which move in shoals have specific size, because the largest are selected for death. by the animals which prey on them. An animal which preyed exclusively on Gammarus, one by one, would also have specific size ; Lankester (loc. cit., p. 41) points out the advantage of small size to a species which feeds on small things singly. Whales have specific size (*Proc. Linn. Soc.*, 1925, p. 18), possibly related to their feeding, possibly inherited from their active flesh-eating land ancestors.)

THE EXPERIMENTAL STUDY OF SENESCENCE *

BY

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Conclusive evidence regarding problems of senescence is very scarce. This is mainly due to the fact that most of the numerous experiments which have been performed deal with isolated cases, few workers having had the opportunity of carrying out observations and experiments on a group of animals sufficiently large and sufficiently homogeneous to permit the collection of decisive data.

ANIMAL STOCK USED

At present such an opportunity exists, and is used to some extent, in this laboratory. The present writer imported, three years ago, some pairs of Wistar rats from which a " standard " stock was bred. Most of the stock, which is maintained at a strength of approximately 3,000 animals, has been derived from one ancestral pair by continuous litter-brother by litter-sister mating. The rest of the stock is as highly inbred as the sex ratio of the litters of the early generations permitted. The environmental conditions are kept as constant as possible, the animals being housed in standard cages in a special building fitted with thermostatic central heating and a cooling device. No artificial selection has been applied to the stock. The control half of the stock is permitted to die off without interference save in certain cases such as mammary tumours, which are very frequent in our colony, bites, skin and hair parasites. Individual records are kept of all stock animals, the cages being examined daily.

The stock was used during the last two years for a number of endocrinological, nutritional, and behaviour experiments. The Edinburgh stock has in common with the original Philadelphia stock certain advantages and shortcomings. Early growth is rapid, mortality during the first eighteen months of life is low, and resistance to infection high ; on the other hand, emaciation after the eighteenth month of life is frequent, when many animals die without showing consistently specific pathological changes. Also, the duration of life, both average and maximum, appears to be rather short.

It will not be possible to publish adequate vital statistics or conclusive experimental data before the end of 1933 ; at present only a few preliminary notes can be given, and it will have to be remembered that these notes refer to animals of the first generation. It will have to be taken into account that the animals of successive generations are not absolutely comparable with each other since the degree of inbreeding obviously increases with each generation, and it remains to be determined to what extent this factor influences the mortality rate and other important characteristics. The oldest age observed in the male was 1,004 days, in the female 982 days. This is considerably below the maximum ages recorded by previous breeders.

* Read in opening a discussion in the Section of Comparative Medicine at the Centenary Meeting of the British Medical Association, London, 1932.